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| 10/527,271 | 03/08/2005 | Alan Crossman | G & C 184.4-USWO | 3503 |

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| EXAMINER | |
|---|---|
| JAVANMARD, SAHAR | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/527,271 | CROSSMAN ET AL. | |
| | Examiner | Art Unit | |
| | SAHAR JAVANMARD | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *26-50* is/are pending in the application.

4a) Of the above claim(s) *38 and 46-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-37,39-45 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/8/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

This Office Action is in response to Applicant's Restriction Requirement remarks filed on April 23, 2008. Claim(s) 26-50 are pending. Claim(s) 38 and 46-49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant's election of species of (1) Tofisopam as the species of genus compound; and (2) parkinsonism as the species of disorder or agent associated with dyskinesia with traverse of the restriction requirement in the reply is acknowledged.

The traversal is on the grounds that there is no serious burden on the Examiner to collectively examine the different claim groups.

Examiner respectfully notes that if the elected species are found free of the art, the search will be expanded to encompass the other species claimed.

The requirement is deemed proper and is therefore made FINAL. Claim(s) 26-37, 39-45 and 50 are examined herein insofar as they read on the elected invention and species.

### *Objections*

Claim 36, the word “drug” is misspelled. Appropriate action is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 50 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the treatment of dyskinesia, does not reasonably provide enablement for the prevention/prophylactic treatment of dyskinesia as recited in these claims.

The instant claims are drawn to a method for the prevention/prophylactic treatment of dyskinesia. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant invention pertains to a method for the prevention/prophylactic treatment of dyskinesia.

The state of the prior art:

The skilled artisan would view that the prevention/prophylactic treatment of one or more symptoms of dyskinesia totally, absolutely, or permanently, is highly unlikely, since one cannot guarantee that the dyskinesia will always be prevented.

The relative skill of those in the art:

The relative skill of those in the art is very high.

The predictability or lack thereof in the art:

The skilled artisan would view that preventing/prophylactically treating dyskinesia, absolutely or permanently, is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples:

In the instant case, no working examples are presented in the specification as filed showing how to prevent/prophylactic treat dyskinesia totally, absolutely, or permanently. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

*Genentech, Inc. v. Novo Nordisk*, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the combination in the instant claims whether one can prevent/prophylactically treating dyskinesia totally, absolutely, or permanently.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970).

Chenard teaches a method of treating dyskinesias associated with dopamine agonist therapy in the treatment of a CNS disorder, in particular Parkinson's disease through the administration of an AMPA receptor antagonist (page 2, lines 23-26).

Chenard teaches that dyskinesia means any abnormal or uncontrollable movement including chorea, tremor, dystonia, among others (page 10, lines 50-52).

Further, dopamine agonist therapy refers to therapy that increases dopamine receptor stimulation including bromocriptine and increasing levels of dopamine such as L-dopa among others (page 10, line 54-page 11, line 8).

Chenard does not teach the compounds of Applicant's formula I.

Ling teaches 2,3-benzodiazepines of formula I which are encompassed by Applicant's compounds of formula I (abstract; column 1, line 15- column 2, line 28). Ling teaches the compounds as being non-competitive inhibitors of the AMPA receptors (column 2, lines 30-32). Further, Ling teaches that the compounds can be used for treating neurological and psychiatric disorders that are triggered by overstimulation of the AMPA receptor. The neurological diseases, which can be treated functionally, include, for example, neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease, and Huntington's chorea (column 3, lines 8-15).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have treated dyskinesia with the administration of AMPA antagonists as

taught by Chenard and employed the AMPA antagonists taught by Ling. One would be motivated to employ the compounds of formula I as taught by Ling because they are also taught to be useful in treating neurodegenerative disorders such as Parkinson's disease. Since both references teach the use of AMPA antagonists for treatment associated with Parkinson's disease, one would expect with a reasonable degree of success that the administration of one AMPA antagonist for another, namely the compounds employed by Ling, would be equally successful in treating dyskinesia, in the absence of unexpected results.

Claims 28, 29, 31, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970) as applied to claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 above in further view of Solyom et al. (Current Pharmaceutical Design, May 2002).

Chenard and Ling are discussed above.

Neither Chenard nor Ling teach the specific compounds of Applicant's formula I that are encompassed by claims 28, 29, 31, and 32, namely Tofisopam.

Solyom teaches 2,3-benzodiazepine derivatives, specifically Tofisopam, as non-competitive AMPA antagonists.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have treated dyskinesia with the administration of AMPA antagonists as taught by Chenard and employed 2,3-benzodiazepines AMPA antagonists as taught by Ling, namely Tofisopam. See discussion above. One would be motivated to employ

Tofisopam because it is also a 2,3-benzodiazepines AMPA antagonist. Thus one would expect with a reasonable degree of success that the administration of one 2,3-benzodiazepines AMPA antagonist for another, namely Tofisopam, as taught by Solyom would be equally successful in treating dyskinesia, in the absence of unexpected results.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chenard et al. (EP 0900568 A2) in view of Ling et al. (US Patent 6,200,970)as applied to claims 26, 27, 30, 33-34, 36-37, 39 and 41-45 above in further view of http://web.archive.org/web/20000815082545/neurologychannel.com/parkinsonsdisease/index.shtml (referred to as "PD website" heretofore).

Chenard and Ling are discussed above.

Neither Chenard nor Ling specifically teach the type of parkinsonism (i.e., idiopathic Parkinson's disease).

The "PD website" teaches that the most common type of Parkinson's disease is idiopathic Parkinson's disease because the cause is unknown.

It would have been obvious to one of ordinary skill in the art at the time of the invention that employing the treatment of dyskinesia associated with parkinsonism as discussed above, that one would have necessarily been treating idiopathic Parkinson's disease. The motivation, provided by the PD website, teaches that idiopathic Parkinson's disease is the most common type of the disease.

***Conclusion***

Claims 26-37, 39-45 and 50 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sahar Javanmard whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617